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EXAMINER	
SWITZER, JULIET CAROLINE	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 03/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

JRL

Office Action Summary	Application No.	Applicant(s)	
	10/057,275	COLEMAN ET AL.	
	Examiner	Art Unit	
	Juliet C. Switzer	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 June 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18,20,23 and 62-66* is/are pending in the application.

4a) Of the above claim(s) *1,2,11,14-18,20 and 23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-10,12,13 and 62-66* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This action is written in response to applicant's correspondence submitted 12/20/04. Claims 1-18, 20, 23, and 62-66 are pending. Claims 1-2, 11, 14-18, 20, and 23 are withdrawn from prosecution as being drawn to non-elected inventions. In the paper filed 6/14/04, claims 3, 4, 9, 10, 12, 62, 65, and 66 were amended. Claims 3-10, 12-13, and 62-66 are under examination herein. Applicant's amendments and arguments have been thoroughly reviewed, but are not persuasive for the reasons that follow. Any rejections not reiterated in this action have been withdrawn. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Priority

2. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application); the disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994). In the instant case, the amendments to the claims introduce the phrase "having at least 97% sequence identity to the amino acid sequence of SEQ ID NO: 4" which is not supported by written description in the prior application or in this application (see New Matter rejection herein). Therefore, since claims 3, 6, 7, 8, 9, 10, 62, 63, 64, and 65

contain language that does no have support in the parent application, priority is not granted to the parent application for these claims.

3. Applicant is required to (A) file a new oath or declaration along with the surcharge set forth in 37 CFR 1.16(e) and (B) redesignate the current application as a continuation-in-part (see MPEP 201.06(c)(III)).

Claim Rejections - 35 USC § 112- New Matter

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

(A) The previously set forth rejection of claims 9, 10, and 65, concerning the limitations of "has an insertion or deletion of 1-5 amino acids as compared with SEQ ID NO: 4" and/or "has one or more amino acid substitutions as compared with SEQ ID NO: 4, and has the amino acid sequence of SEQ ID NO: 4 at amino acids 1, 4, 6, 7, 10, etc..." is WITHDRAWN in view of either the cancellation of the subject matter OR the specific basis for the language as present on page 6, last full paragraph of the specification.

(B) The rejection of claims 60 and 61 for new matter is moot in view of the cancellation of these claims.

(C) Claims 3, 6, 7, 8, 9, 10, 62, 63, 64, and 65 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a

way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. MPEP 2163.06 notes "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. In re Rasmussen , 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)."

The amended claims recite the limitation "wherein the variant shares at least 97% sequence identity with SEQ ID NO: 4," and this language is new matter in view of the specification. Applicant argues that support for amended independent claims 3, 9, and 62 can be found implicitly on page 6 of the specification in the final full paragraph (p. 8 of remarks). Applicant further argues that the insertion of a requirement that the variant shares "at least 97% sequence identity with SEQ ID NO: 4" is supported because the specification states that the polypeptides of the present invention may comprise an insertion or deletion of 1 to 5 amino acids. Applicant asserts that since changing 1 to 5 amino acids in SEQ ID NO: 4 would result in a modified sequence sharing "approximately 97% to 100% sequence identity with SEQ ID NO: 4", the amendment is implicitly supported (see remarks, p. 9).

This is not persuasive.

Five amino acid substitutions in a 134 bp sequence (assuming substitutions) would result in a sequence that is 96.2% (or 96%) identical to SEQ ID NO: 4. This is not basis for 97% identity, even if the specification were to discuss the number of possible substitutions that could be present in variants. However, the specification does not state any particular number of substitutions that are allowed within variant sequences. The specification states " 'Insertions' or 'deletions' are typically in the range of about 1 to 5 amino acids." The literal "97% sequence

identity" language is clearly not supported by the specification, but neither is the language "implicitly" supported as applicant asserts. While it is true that one yard is equal to three feet, a deletion of five amino acids in a 134 base pair sequence does not equal a statement of 97% sequence identity. Alignment of sequences with insertions and deletions is highly dependent upon the scoring parameters used in the alignment algorithm. For example, using a ClustalW alignment program on default parameters, five deletions were made throughout SEQ ID NO: 4. Then the deleted sequence was aligned to the original SEQ ID NO: 4. The program calculated that the two sequences have 94% identity.

```
CLUSTAL W (1.82) multiple sequence alignment
SeqA Name        Len(aa)  SeqB Name        Len(aa)  Score
=========================================================
1    seqid4      129      2    deletions   134      94
=========================================================

seqid4           MAQSLAL-LLILVLAFGIPRTQGSDG-AQDCCLKYSQRKIPAKVVRSYRKQEPSLGCSIP 58
deletions        MAQSLALSLLILVLAFGIPRTQGSDGGAQDCCLKYSQRKIPAKVVRSYRKQEPSLGCSIP 60
                 ******* ****************** ********************************

seqid4           AI-FLPRKRSQAELCADPKELWVQQLMQ--DKTPSPQKPAQGCRKDRGASKTGKKGKGSK 115
deletions        AILFLPRKRSQAELCADPKELWVQQLMQHLDKTPSPQKPAQGCRKDRGASKTGKKGKGSK 120
                 ** ************************  ******************************

seqid4           GCKRTERSQTPKGP 129
deletions        GCKRTERSQTPKGP 134
                 **************
```

Using different parameters (GapExtension 2.5, GapDistance 1), however, an alignment of the same sequences is obtained in which the sequences are determined to have only 90% identity.

```
SeqA Name             Len(aa)  SeqB Name             Len(aa)  Score
=============================================================
1    seqid4           129      2    fivedeletions    129      90
=============================================================

seqid4             MAQSLAL-LLILVLAFGIPRTQGSDG-AQDCCLKYSQRKIPAKVVRSYRKQEPSLGCSIP 58
fivedeletions      MAQSLALSLLILVLAFGIPRTQGSDGGAQDCCLKYSQRKIPAKVVRSYRKQEPSLGCSIP 60
                   ******* ****************** ********************************

seqid4             AI-FLPRKRSQAELCADPKELWVQQLMQ--DKTPSPQKPAQGCRKDRGASKTGKKGKGSK 115
fivedeletions      AILFLPRKRSQAE-----KELWVQQLMQHLDKTPSPQKPAQGCRKDRGASKTGKKGKGSK 115
                   ** **********     **********  ******************************

seqid4             GCKRTERSQTPKGP 129
fivedeletions      GCKRTERSQTPKGP 129
```

****

Further, it is noted that the portion of the specification relied upon does not limit the number of insertions or deletions of one to five amino acids that can be present within variants of the disclosed sequences. That is, while the specification suggests that an insertion or deletion may be between one and five amino acids, it does not state or even suggest that variants would only have a single insertion or deletion.

Thus, even in view of applicant's arguments, the amended claims are rejected for incorporating new matter.

Claim Rejections - 35 USC § 101/112 1st, Lack of Utility

5. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

6. Claims 3-10, 12, 13, and 62-66 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

The claims are drawn to isolated polynucleotides encoding instant SEQ ID NO: 4 or a variety of variants and/or fragments of instant SEQ ID NO: 4 which have "chemokine activity" or which are "immunogenically active fragments." The claims further recite constructs comprising these nucleic acids, including vectors and host cells/organisms, as well as methods for producing polypeptides which utilize these constructs.

The specification teaches that instant SEQ ID NO: 3 encodes instant SEQ ID NO: 4, a polypeptide referred to in the specification as PANEC-2. The specification teaches that PANEC-

2 is a human pancreatic protein that is a member of the C-C chemokine family, based on the fact that the molecule was isolated from a library obtained from human pancreatic tissue and based on homology of SEQ ID NO: 4 to other C-C chemokines.

The specification asserts that PANEC-2 is specifically expressed in pancreas, and because of this PANEC-2 nucleic acids are useful in assays based on chemokine production in cases of inflammation or disease affecting the pancreas (p. 8). While asserted utility is specific, it is not substantial. It is not substantial because further experimentation would be required to reasonably confirm that in fact a real world utility exists wherein these molecules can be used in diagnostics.

Chemokines are chemoattractant cytokines. In a 1994 review of chemokines, Schall *et al.* teach that "Although the properties of these molecules have only recently begun to be elucidated, the bulk of the evidence to date suggests that the chemokines function as regulators of inflammatory and immunoregulatory processes, particularly through their leukocyte chemoattractant effects (p. 4, third paragraph, as cited in the IDS)." A "leukocyte" is a white blood cell, and includes among its members monocytes, neutrophils, basophils, eosinophils, and lymphocytes, each of which function differently within the body's immune system. Furthermore, Schall *et al.* provide a table which summarizes different sources and targets for the known C-C type chemokines (Table V). Some of these, for example MCP-1, can be isolated from many tissues, while others can be isolate from only T cells (for example I-309). Likewise, with regard to targets, some of the C-C type chemokines target a wide variety of cells, for example MIP-1α targets a variety of leukocytes as well as stem cells, osteoclasts, and hypothalamus. And for some the target is yet unknown, such as the murine C-C chemokine C10.

Furthermore, Schall *et al.* teach that even chemokines with a great deal of structural homology (70%) demonstrate distinct specificities for their cellular targets (p. 16, first full paragraph), and that attempts to even elucidate the targets of chemokines contain "pitfalls of interpretation (p. 23, second paragraph)." The pancreas is a complex organ with many cell types- the specification does not provide any information as to what type of cells produce or are targeted by PANEC-2. Thus, in the instant case, while applicant may have identified a C-C type chemokine, this designation does not speak specifically to the functioning of the molecule with regard to target, and further experimentation (which is unpredictable) would be required to determine such a target. Without knowledge of such a target, it would be difficult to utilize the instant molecule in diagnostics or prognostics because it is unknown what the presence of the molecule would indicate or suggest.

Furthermore, the instant specification asserts that the PANEC-2 molecule is "specifically" expressed in pancreas and can therefore be used in assays to detect diseases or inflammation of the pancreas. However, the specification does not provide any evidence of this specific expression, only teaching that the molecule was isolated from a human pancreatic cDNA library, but never assaying additional tissue types to determine the specificity of expression. Accordingly, the assertion that PANEC-2 is "specifically" expressed in the pancreas is not substantial. All that can be concluded based upon the specification as filed is that PANEC-2 is expressed in pancreas, not that such expression is specific to pancreas. Indeed, the post-filing date art suggests that the PANEC-2 molecule (SEQ ID NO: 4) is expressed in a wide variety of tissues, including lymph nodes, appendix, heart, small intestine, colon, and spleen (Nagira *et al.*, 1997, figure 3). This reference supports the position that at the time the invention was made

further experimentation would have been necessary to even reasonably confirm the expression specificity of the instant molecule.

The specification does not elucidate or demonstrate any particular target for the instantly disclosed chemokine, but instead teaches that excessive expression of PANEC-2 "can" lead to activation of monocytes, macrophages, basophils, eosinophils, T lymphocytes, and/or other cells which respond to chemokines. The language of the specification appears to be prophetic, and suggests that PANEC-2 may activate any one of these or some other undisclosed molecule, but it is equally suggestive that it may not activate any one of these. This is not a definitive assertion of functionality or utility. It is also noted that chemokines are particularly discussed in the specification at several citations regarding their broad activities. For example, on pages 2-3, various chemokines are described with varying activities discussed. Particular attention is drawn to page 3, line 9, wherein it is stated that chemokine activities demonstrate a high degree of target cell specificity. This statement is significant in that the subject matter of the instant claims is "not" characterized as target cell specificity other than the generic pancreas location thereof. Numerous activities are carried out by the pancreas, including numerous non-chemokine activities, and thus this pancreas specificity is generic in nature, especially since the chemokines encoded by the instantly claimed nucleic acids have no asserted correlation to any particular disease or illness, but rather only speculated as being involved in a long list of diseases or illnesses. Thus, the asserted utility of the claimed PANEC-2 encoding nucleic acids as a tool in diagnostics is not substantial because the specification does not teach or suggest the "inflammatory or disease" affecting the pancreas that can be identified using these molecules. Instead, the disclosure of the specification is an invitation to the skilled artisan to attempt to

discover such a disease that is associated with the instantly claimed nucleic acids, and can thus be detected in a diagnostic which utilizes these nucleic acids. Thus, "real world" disease or illness condition correlation is absent for the claimed subject matter, and the asserted utility of the instant nucleic acids in diagnostic applications is not substantial.

The specification further asserts a number of additional possible utilities for the claimed nucleic acids, including as hybridization probes, as oligomers for PCR, use for chromosome and gene mapping, use in the recombinant production of PANEC-2, and use in the generation of anti-sense DNA or RNA, their chemical analogs, and the like (p. 8, third full paragraph). These utilities are not specific because they can generally be applied to any nucleic acid that encodes a protein, of which there are millions of possibilities. Further, these utilities are not substantial. For example, a nucleic acid may be utilized to obtain a protein. The protein could then be used in conducting research to functionally characterize the protein. The need for such research clearly indicates that the protein and/or its function is not disclosed as to a currently available or substantial utility. A starting material that can only be used to produce a final product does not have substantial asserted utility in those instances where the final product is not supported by a specific and substantial utility. In this case none of the proteins that are to be produced as final products resulting from processes involving claimed nucleic acid have asserted or identified specific and substantial utilities. The research contemplated by applicants to characterize potential protein products, especially their biological activities, does not constitute a specific and substantial utility. Identifying and studying the properties a protein itself or the mechanisms in which the protein is involved does not define "real world" context or use. Similarly, the other listed and asserted utilities as summarized above or in the instant

specification are neither substantial nor specific due to being generic in nature and applicable to a myriad of such compounds.

Neither the specification as filed nor any art of record discloses or suggests any property or activity for the nucleic acid and/or protein compounds such that another non-asserted utility would be well established for the compounds. In the instant specification in the fourth full paragraph on page 4, applicants set forth a research proposal for "new diagnostic techniques" and for "use in the development of effective therapies." This statement in itself appears to be an invitation to conduct further research to reasonably confirm that a specific and substantial utility exists for the claimed molecules. It is noted that a number of examples have been set forth for the basic isolation and characterization of PANEC-2 starting in the instant specification on pages 13-15. From pages 16-26 of the specification a review of generic methods are given with only speculation as to what specific or substantial effects are connected to PANEC-2. These are also clearly research proposals which lack patentable utility. In summary, the instant invention, as filed, has not been set forth with a patentable utility due to a lack of specific, substantial, or well established utility.

Claims 1-10, 12, 13, 60, 61, and 62-65 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 USC § 112-Written Description

7. Claims 3, 6-8, 9, 13, 62, 64, 65, and 66 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject

matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Rejected claim 3 is drawn to isolated polynucleotides encoding a polypeptide consisting of the amino acid sequence of SEQ ID NO: 4, or a polypeptide that is a variant of SEQ ID NO: 4, wherein said variant shares at least 97% sequence identity with SEQ ID NO: 4, and the variant has chemokine activity, or a biologically active fragment of a polypeptide consists of the amino acid sequence SEQ ID NO: 4, wherein said fragment has chemokine activity, or an immunogenic fragment of a polypeptide that consists of the amino acid sequence of SEQ ID NO: 4, wherein the fragment is capable of generating an antibody that specifically binds to the polypeptide of SEQ ID NO: 4, and the immunogenic fragment possesses biological activity.

The subject matter of part (a) is adequately described.

The subject matter of part (b) includes nucleic acids that encode variants of SEQ ID NO: 4 which are not described in the specification, including nucleic acids which encode molecules from other species of related animals, allelic variants, splice variants and the like. Further, the claims do not recite a requisite structure/function relationship between a recited function in the claims and a function of the encoded amino acid. Though the claim recites that the encoded variant must have "chemokine activity" this recitation of function is very broad, as chemokines are known to be active in a variety of ways, as proteins that bind to receptors that then transmit a wide variety of possible signals within a cell. There is no clear relationship between the structure recited in part (b) of the claim and the recited "function."

Considering part (c) the polynucleotide of claim 3, this genus of nucleic acids is also quite broad, because while the claim requires that the encoded fragment be "biologically active" and have "chemokine activity" this could include any number of possible amino acid residues. Since these two recited functions are broad in their nature (biological activity encompassing even an activity such as being a substrate for a protease or the ability to raise an antibody), these functions do not help to define the claimed genus. Furthermore, the specification does not discuss which fragments of SEQ ID NO: 4 are essential for the maintenance of "chemokine activity" a fact that is particularly relevant in view of the fact that the specification does not even demonstrate what type of chemokine activity SEQ ID NO: 4 possesses to begin with. Furthermore, the claim is open in nature, requiring only that the claimed polynucleotide encode a fragment of SEQ ID NO: 4 that meets the functional language of the claim, but that polynucleotide could further encode other fragments flanking the fragment of SEQ ID NO: 4, and so the claimed polynucleotide encompasses polynucleotides that encode related chemokines, allelic variants not disclosed, as well as possible splice variants of the disclosed nucleic acid.

Part (d) of claim 3 encompasses any nucleic acid encoding any immunogenically active fragment of SEQ ID NO: 4 wherein the fragment is "capable" of generating an antibody that "specifically binds" to SEQ ID NO: 4. The specification at page 12 teaches that antibodies inherently specifically bind their target as opposed to other target sequences, and so in this case, the language "specifically binds" is quite broad in nature and does not provide a defining characteristic, as any antibody raised by a fragment of SEQ ID NO: 4 would specifically bind some portion of SEQ ID NO: 4. Furthermore, the claim is open in nature, requiring only that the claimed polynucleotide encode a fragment of SEQ ID NO: 4 that meets the functional language

of the claim, but that polynucleotide could further encode other fragments flanking the fragment of SEQ ID NO: 4, and so the claimed polynucleotide encompasses polynucleotides that encode related chemokines, even polypeptides that are not chemokines but share some amino acid sequence in common with SEQ ID NO: 4, allelic variants not disclosed, as well as possible splice variants of the disclosed nucleic acid. The genus of nucleic acids encompassed within this claim includes a wide variety of polynucleotides encoding amino acid sequences that are not described.

Claims 6-8 are drawn to constructs and methods that utilize or comprise nucleic acids of claim 3.

Claim 9 is an independent claim and encompasses fragments and variants of SEQ ID NO: 4, in particular. The language used in claim 9 is very similar to that used in claim 3, and an analogous analysis applies to the various sections of this claim.

Claim 13 claims an isolated polynucleotide comprising at lest 60 contiguous nucleotides of a polynucleotide of SEQ ID NO: 3. Claim 13 is drawn using broad "comprising" language, and encompasses polynucleotide fragments of 60 nucleotides with any potential flanking sequences. The claim has no functional requirement. The claim thus encompasses any number of splice or allelic variants of SEQ ID NO: 3, as well as potential genomic sequences any of which encode molecules with any potential function.

Claims 62, and 64-65 are drawn to isolated polynucleotide sequences encoding a polypeptide that comprises an amino acid sequence having at least 97% sequence identity to the amino acid sequence of SEQ ID NO: 4 and possessing chemokine activity. The claims encompass nucleic acids that encode variants of SEQ ID NO: 4 which are not described in the specification, including nucleic acids which encode molecules from other species of related

animals, allelic variants, splice variants and the like. Further, the claims do not recite a requisite structure/function relationship between a recited function in the claims and a function of the encoded amino acid. Though the claim recites that the encoded variant must have "chemokine activity" this recitation of function is very broad, as chemokines are known to be active in a variety of ways, as proteins that bind to receptors that then transmit a wide variety of possible signals within a cell. There is no clear relationship between the structure recited in part (b) of the claim and the recited "function."

Claim 66 recites an isolated polynucleotide that encodes a polypeptide variant of SEQ ID NO: 4, wherein the variant has conservative amino acid substitutions and possesses chemokine activity. The claim requires that the encoded polypeptide has "one or more" conservative amino acid substitutions relative to SEQ ID NO: 4, but does not limit the number of conservative amino acid substitutions relative to SEQ ID NO: 4 and does not exclude any other potential modification relative to SEQ ID NO: 4. Thus, the claim has only minimal structural requirement and encompasses encompasses any molecule discovered or undiscovered that has any potential "chemokine" activity, provided it has at least one conservative amino acid substitution.

Within the genus of the claimed polynucleotides, the instant specification describes only nucleic acids encoding SEQ ID NO: 4, with a particular example of a nucleic acid comprising instant SEQ ID NO: 3. Molecules that consist of fragments of SEQ ID NO: 3 are also described, as are molecules that encode amino acids sequences consisting of fragments of SEQ ID NO: 4. As discussed, however, the claims encompass any number of variants and sequences related to SEQ ID NO: 3 and encoding polypeptides related to SEQ ID NO: 4 that are not described in the specification. It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that

> "...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

In the instant application, only the nucleic sequence of the disclosed SEQ ID NO: 3 and encoding SEQ ID NO: 4 are described. Also, in Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), it was concluded that:

> "...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

In the application at the time of filing, there is no record or description which would demonstrate conception of any nucleic acids encoding proteins modified by addition, insertion, deletion, substitution or inversion with the disclosed SEQ ID No: 4 therefore possessing one or more amino acid differences such that a different amino acid sequence is encoded which retains same function as SEQ ID NO: 4, which function is not clearly set forth in the specification.

Claim Rejections - 35 USC § 112, 2nd Paragraph

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claim 64 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

All previously set forth 112 2nd rejections that are not reiterated or specifically addressed were overcome by applicant's amendments to the claims.

Claims 64 is indefinite because it recite "having one or more conservative amino acid substitution(s)" but they do not recite a reference sequence with which the substitutions are relative to, and therefore it is indefinite as to how to determine if the substitutions are present.

Claim Objections

10. The previously set forth claim objections are overcome by amendment.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 3, 6-9, and 66 are rejected under 35 U.S.C. 102(b) as being anticipated by Caput *et al.* (WO 92/09629).

For applicant's convenience it is noted that the PCT application represented by this WO publication matured into a 371 application filed in the United States which issued as US 6001649. This US Patent provides an English language translation of the French PCT relied upon in this rejection.

Caput *et al.* teach an isolated nucleic acid encoding a biologically active fragment of a polypeptide that consists of the amino acid sequence of SEQ ID NO: 4 wherein said fragment is has chemokine activity. The specification does not define "chemokine activity." This limitation, broadly interpreted includes any activity that a chemokine would possess, such as the ability to raise an antibody that would bind to a portion of a chemokine. Caput *et al.* teach a

polynucleotide that encodes residues 75-78 of SEQ ID NO: 4, and this four amino acid fragment would be immunogenically active, that is able to raise an antibody. The raised antibody would specifically bind to this portion of SEQ ID NO: 4. The specification at page 12 teaches that antibodies inherently specifically bind their target as opposed to other target sequences, and so in this case, the language "specifically binds" is quite broad in nature and essentially applies to any antibody that would bind a target sequence, as any antibody raised by a fragment of SEQ ID NO: 4 would specifically bind some portion of SEQ ID NO: 4. Further, this fragment possesses biological activity insofar as it can raise an antibody, be bound by an antibody or be the substrate for a protease. Thus, the nucleic acid taught by Caput *et al.* meets at least the limitations of claim 3 as recited in part (c) and further encodes the polypeptide recited in claim 9(c).

Caput *et al.* teach an isolated nucleic acid encoding a chemokine.

With regard to claim 6, Caput *et al.* teach recombinant polynucleotides comprising a promoter sequence operably linked to their SEQ ID NO: 15 and, with regard to claims 7 and 8, they teach host cells which are transgenic organisms comprising the recombinant polynucleotides.

With regard to claim 9, Caput *et al.* teach a method for producing the polypeptide encoded by their SEQ ID NO: 15, which comprises culturing a cell under conditions suitable for the expression of the polypeptide, and recovering the polypeptide (Sections 5-7, pages 31-44).

With regard to claim 66, the polynucleotide taught by Caput *et al.* is a sequence encoding a variant which has many conservative amino acid substitutions as well as other substitutions relative to SEQ ID NO: 4 and possesses chemokine activity. The claim does not set forth any

limitations to the number of substitutions present in the encoded "variant", it only requires that the encoded variant have one or more conservative amino acid substitution.

Thus, the teachings provided by Caput *et al.* meet all of the limitations of the rejected claim.

```
Qy          1 MetAlaGlnSerLeuAlaLeuSerLeuLeuIleLeuValLeuAlaPheGlyIleProArg 20
              |||       |||    ||||||       |||:::|||       |||          |||:::
Db         71 ATGAAAGCCTCTGCAGCACTTCTGTGTCTGCTGCTCACAGCAGCTGCTTTCAGCCCCCAG 130

Qy         21 ThrGlnGlySerAspGlyGly---------AlaGlnAspCysCysLeuLysTyrSerGln 37
                              |||          :::       ||||||    ::::::
Db        131 GGGCTTGCTCAGCCAGTTGGGATTAATACTTCAACTACCTGCTGCTACAGATTTATCAAT 190

Qy         38 ArgLysIleProAlaLysValValArgSerTyrArgLysGlnGluProSerLeuGlyCys 57
              :::|||||||||    :::    :::    |||||||||:::          |||       |||
Db        191 AAGAAAATCCCTAAGCAGAGGCTGGAGAGCTACAGAAGGACCACCAGTAGC---CACTGT 247

Qy         58 SerIleProAlaIleLeuPheLeuProArgLysArgSerGlnAlaGluLeuCysAlaAsp 77
                    |||::::::|||       :::    :::          |||:::||||||||||
Db        248 CCCCGGGAAGCTGTAATCTTC------AAGACCAAACTGGACAAGGAGATCTGTGCTGAC 301

Qy         78 ProLysGluLeuTrpValGlnGlnLeuMetGlnHisLeuAsp---LysThrProSerPro 96
              |||    :::    |||||||||       |||:::|||||||||    ||||||    :::|||
Db        302 CCCACACAGAAGTGGGTCCAGGACTTTATGAAGCACCTGGACAAGAAAACCCAAACTCCA 361

Qy         97 Gln 97
              :::
Db        362 AAG 364
```

13. Claims 3, 6, 7, 8, 9, 10, 62, 63, 64, and 65 are rejected under 35 U.S.C. 102(b) as being anticipated by Hromas *et al.* (J. Immunol 159(6)2554-2558 (1997)), as evidenced by GenBank Accession number U88320 (18 December 1997).

Hromas *et al.* is available as prior art for this rejection because the rejected claims are not entitled to priority under 120 to the parent application because they all include subject matter that is not supported by the specification of the parent application (see heading "Priority" in this office action).

Hromas *et al.* teach the isolation of a cDNA sequence containing the entire open reading frame of a molecule referred to therein as human Exodus-2 (p. 2554, 2nd column, heading "Isolation"). Hromas *et al.* teach that the sequence was submitted to GenBank as accession U88320. Nucleotides 15-416 of this molecule encode instant SEQ ID NO: 4.

Therefore, with regard to claim 3, Hromas *et al.* teach an isolated polynucleotide encoding a polypeptide consisting essentially of the amino acid sequence of SEQ ID NO: 4.

With regard to claims 6, 7, and 8, Hromas *et al.* teach that the complete cDNA was cloned into an expression vector and isolation of the protein from sF9 cells. With regard to claims 9 and 10, Hromas *et al.* teach culturing the cell to express the polypeptide and recovering the polypeptide (p. 2555, 1st column, Recombinant Exodus-2 production).

With regard to claim 62, Hromas *et al.* teach an isolated polynucleotide encoding a polypeptide that comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence of SEQ ID NO: 4 and possesses chemokine activity.

With regard to claim 63, the polynucleotide encodes a polypeptide consisting essentially of SEQ ID NO: 4.

With regard to claim 64, the polynucleotide encodes a polypeptide having one or more conservative amino acid substitutions. The reference is applied to this claim because the claim does not set forth a reference sequence that the substitutions are relative to, and relative to some arbitrary chemokine sequence there are any number of conservative amino acid substitutions, depending on the sequence.

With regard to claim 65, the polynucleotide encodes a polypeptide that has zero deletions compared with SEQ ID NO: 4. The claim is indefinite but this rejection is written against a

claim that requires about 1 to 5 amino acid deletions compared with SEQ ID NO: 4. Hromas *et al.* teach a polynucleotide encoding a polypeptide having zero deletions, which is "about 1."

Therefore, the teachings of Hromas *et al.* anticipate each of the rejected claims.

Response to Remarks

New grounds of rejection are set forth to address the amendments to the claims.

The **written description rejection** is modified and maintained to address the amended claims. The rejection is overcome by amendment for any claims for which the rejection is not reiterated.

Applicant traverses the rejection beginning on page 11, section VII of the response. Applicant argues that because of the redundancy in the genetic code and the teachings of the instant application, a skilled artisan would know what amino acids can be changed within SEQ ID NO: 4 to encode a polypeptide that "corresponds" with SEQ ID NO: 4. This is not persuasive if "corresponds with" means that the two polypeptides have the same function, since the function of SEQ ID NO: 4 is not taught in the specification. The specification asserts that SEQ ID NO: 4 has "chemokine activity," which is a broad statement of functionality that varies among even members of this class of proteins, as discussed in the rejection. There is no identification of a particular structure in the specification that is correlative with this function. The specification teaches at example XII how to screen for various different potential chemo attractant activities, but not which ones are possessed by SEQ ID NO: 4. Applicant is in possession of a molecules (SEQ ID NO: 4) and nucleic acids encoding that molecule which certainly possess a particular activity, but applicants have not disclosed what this activity is.

Applicant states that a skilled artisan "would know what amino acid substitutions could be made to SEQ ID NO: 4 so as to preserve the chemokine function of the protein." This statement is not supported by facts or evidence on the record, especially since "the" chemokine function of the protein is unknown.

Applicant argues at page 12, that one could asses the immunogenic or biological activity of fragments of SEQ ID NO: 4. The written description rejection is set forth against these claims insofar as they are not limited to isolated nucleic acids consisting of polynucleotide that encode amino acids consisting of fragments of SEQ ID NO: 4, but instead include flanking sequences which are not described and lead to the claim encompassing any number of variants as well as genomic sequences, etc.

With regard to claim 66, applicant argues that the claim refers now to SEQ ID NO: 4. This is not persuasive for the reasons discussed in the rejection of the amended claim.

Therefore, even in view of applicant's remarks, the rejection is MAINTAINED.

The **112 2nd rejection** is maintained for claim 64. Applicant argues that the claim is clear because it depends from claim 62 which recites an nucleic acid encoding a variant that shares at least 97% identity with SEQ ID NO: 4 (response page 12, section VII). This is not persuasive because the claim is still not clear if the "one or more conservative amino acid substitutions" are relative to SEQ ID NO: 4 or relative to some other unnamed chemokine.

The rejection for **lack of utility** is maintained.

Applicnat argues that the assertion that the polynucleotides of the claimed invention encode "pancreatic expressed chemokines" is a specific and substantial utility (response page 10, section VI). As discussed in the rejection, the classification of a molecule as a "chemokine" with no further description of the target of the chemokine is not a specific and substantial utility. The specification teaches that excessive expression of PANEC-2 "can" lead to activation of monocytes, macrophages, basophils, eosinophils, T lymphocytes, and/or other cells which respond to chemokines. There is no disclosure that this in fact happens or which of the list of potential targets would be activated. Further with regard to the designation of the molecule as "pancreatic" the specification teaches that the molecule was isolated from a human pancreatic cDNA library, but provides any study of additional tissue types to determine the specificity of expression. Accordingly, the assertion that PANEC-2 is "specifically" expressed in the pancreas is not substantial. All that can be concluded based upon the specification as filed is that PANEC-2 is expressed in pancreas, not that such expression is specific to pancreas.

Applicant refers to the post-filing date art as teaching that the instantly claimed nucleic acid molecules encode a chemokine that is chemotactic for lymphocytes. This assertion is not in the instant specification. The instant specification provides only a laundry list of potential targets for the encoded chemokine with no further guidance as to which target from the list is the actual target. As plainly stated in MPEP 2164.05(a), the specification must be enabling as of the filing date. In the specification as originally filed, there is an assertion that the claimed nucleic acid "may" encode a polypeptide that could activate one of a list of possible cell types, and that list even includes the open ended designation "or other cells which respond to chemokines." Applicant argues at page 11 of the response that applicant does not have to show which cells are

specifically activated by the chemokine, arguing that the disclosure that the molecule encodes a "chemokine" is sufficient. This is not persuasive for all of the reasons of record, including, particularly because the designation of a molecule as a "chemokine" is a classification within a broad group of molecules with a variety of activities and functions, similar to the designation of a molecule as a "receptor." Without knowing the target cells for the chemokines, one does not know how to use the claimed molecules. The examiner is only requiring the assertion of a specific, substantial, and credible utility, and for the reasons of record as set forth in these arguments and in the rejection of record, the rejection is MAINTAINED.

With regard to the **102(b)** rejection in view of Caput et al., the rejection is MAINTAINED. Applicant argues that the rejection is overcome with regard to claims 3 and 9 by the amendment to recite that the immunogenic fragment is at least 5 amino acids in length. However, this is not sufficient to overcome claims 3 and 9 in their entirety as the biological fragment recited in part (b) of the claim remains taught by Caput et al., as discussed in the rejection. As discussed in the rejection, "biological activity" as broadly interpreted includes the ability to raise antibodies or be a substrate for a protease, both of which the fragment taught by Caput *et al.* posses.

Applicant does not traverse this rejection with regard to claim 66. The rejection is applied to the amended claim because the claim requires that the "variant" of SEQ ID NO: 4 "have" one or more conservative amino acid substitutions, but does not exclude additional changes relative to SEQ ID NO: 4.

With regard to the rejection in view of Hromas et al. applicant argues at page 14 of the response that Hromas is not available as prior art. However, this is not persuasive because there is not support in the parent application for the limitation of 97% sequence identity present in the rejected claims as previously discussed in this office action. Therefore, the rejection is MAINTAINED.

Conclusion

14. No claims are allowed.

15. Claim 4, 5, 12, and 13 are free of the prior art. These claims are granted priority to the parent application insofar as there is descriptive support in that application for the claims. The prior art does not teach or suggest an isolated polynucleotide encoding SEQ ID NO: 4, and in particular does not teach an isolated polynucleotide comprising instant SEQ ID NO: 3. Further, with regard to claim 13, the prior art does not teach or suggest an isolated polynucleotide comprising at least 60 contiguous nucleotides of SEQ ID NO: 3.

16. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Juliet C Switzer whose telephone number is (571) 272-0753. The examiner can normally be reached on Monday through Wednesday, from 9:00 AM until 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached by calling (571) 272-0745.

The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571)272-0507.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the

problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Juliet C. Switzer
Primary Examiner
Art Unit 1634

March 16, 2005